West Nile Virus Newsletter

Zoonotic Disease Program, Washington State Department of Health

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Purpose

To keep our partners and other interested entities informed about West Nile virus (WNV)

In This Issue

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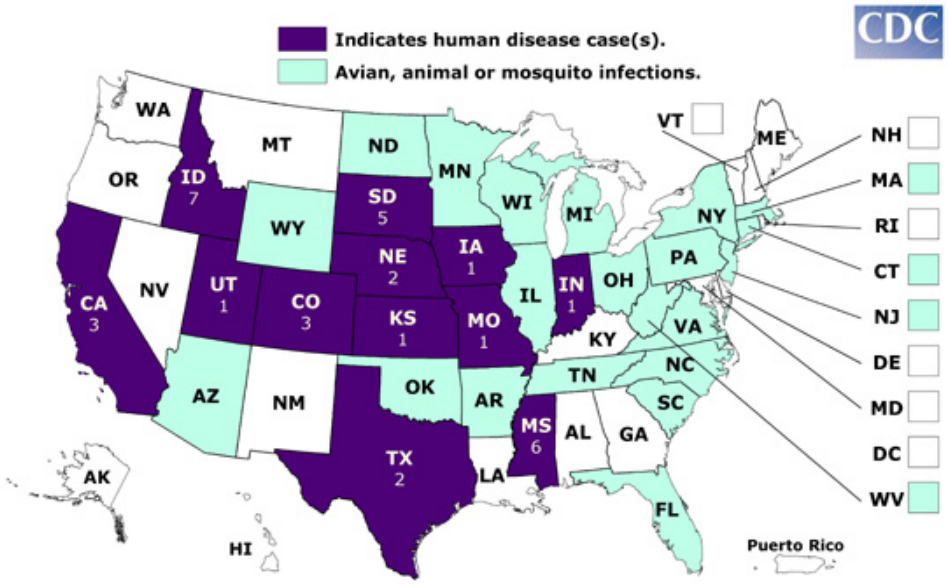
Subscribe, Submit Articles, Suggestions

Contact Ben Hamilton
benjamin.hamilton@doh.wa.gov

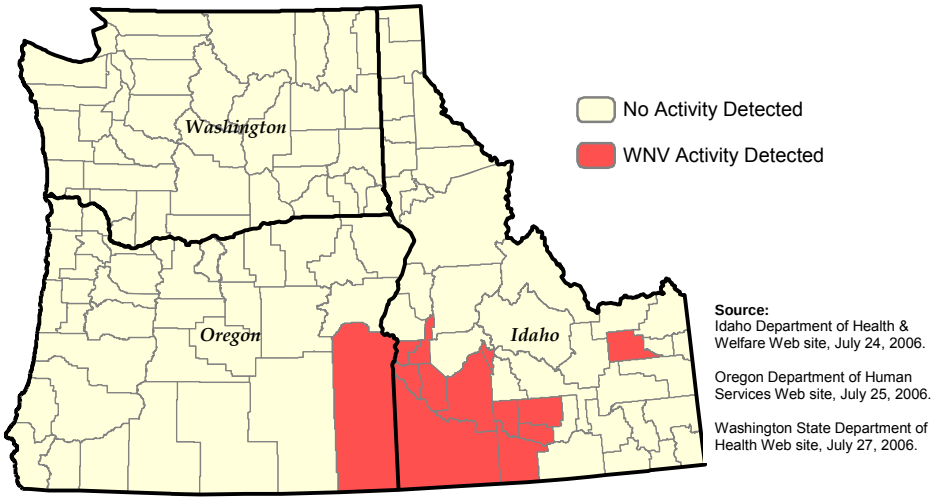
West Nile virus activity in the United States

Surveillance findings reported to CDC, July 25, 2006



National maps and data available at http://www.cdc.gov/ncidod/dvbid/westnile/surv&control.htm.

West Nile virus activity in the northwest, 2006



Idaho currently leads the nation in human WNV cases. Idaho reports detecting eleven people with the virus this year. At this time last year, WNV was detected in just two Idaho counties and there were no human cases. Compare this northwest map with the one a year ago in the July 27, 2005 West Nile Virus Newsletter.

Web Resources

Washington State Department of Health
www.doh.wa.gov/wnv

Centers for Disease Control and Prevention
www.cdc.gov/ncidod/dvbid/westnile

US Geological Survey & CDC ArboNET maps
http://westnilemaps.usgs.gov/index.html

Washington State University Cooperative Extension
www.wnv.wsu.edu

Washington State Department of Agriculture
www.agr.wa.gov/FoodAnimal/AnimalHealth/Diseases/WestNileVirus/default.htm

Northwest Links

Idaho Department of Health & Welfare
www.westnile.idaho.gov

Oregon Department of Human Services
http://egov.oregon.gov/DHS/ph/acd/diseases/wnile/survey.shtml

British Columbia Center for Disease Control
http://www.bccdc.org/content.php?item=183

Keeping the bugs at bay

By Kevin Krajick, Article excerpt from Science, July 7, 2006. 313 (5783): 36-38

Bug-repellent research, long waged on primitive levels and with mixed results, may be looking up. The developed world once viewed repellents chiefly as products for backyard comfort, but with the spread of insect-borne agents such as West Nile virus, they have become a public-health issue. There is also growing recognition that vector-borne diseases routinely devastate the developing world; in Africa alone, 800,000 children die from malaria every year. Expensive research into vaccines, medicines, and genetic modifications to wild insects has so far delivered little, so many scientists are going back to basics: insecticides, bed netting, and repellents.

With new funding initiatives, biologists are using more sophisticated methods to improve understanding of insects' finely evolved olfactory systems and to find substances that might disrupt them. Researchers have uncovered possible new repellents in nature and in the lab, and a few have already made it to market; others may be on the way. "If we can really understand how insects find us, we can figure out how to prevent them from finding us," says Yale University molecular neurobiologist John Carlson, part of a new three-continent team.

Trying to beat DEET: Cultures from ancient Egyptians to modern U.S. Southerners have used remedies as diverse as snakeskin and cow parsnip to keep away pests. But so far the Holy Grail--a compound that bugs hate and humans find pleasant--has been elusive. The central weapon in the modern arsenal is N,N-diethyl-meta-toluamide, or DEET; invented in 1953, it smells evil, melts plastic, and is perceived by many people to be poisonous. No one even quite knows how it works. At 30% concentrations, DEET drives away a broad spectrum of bugs for up to 8 hours, including *Culex pipiens* mosquitoes, which carry West Nile virus. However, many commercial products carry as little as 7% DEET because it's so unpleasant, and even high concentrations fall short against *Anopheles* mosquitoes, which spread malaria, and against ticks, which spread Lyme disease and Rocky Mountain spotted fever. The U.S. military has found that in the fierce heat of Iraq, DEET evaporates quickly. In the current war, biting sandflies have inflicted close to 2000 cases of leishmaniasis, which causes debilitating skin lesions.

Psychology also plays a role. The U.S. Department of Defense recently revived work on new repellents after finding that soldiers often toss out green tubes of military-issue DEET because they fear it is toxic and hate its sticky feel. Some unknowingly replace it with the same stuff in a more colorful package aimed at civilians, says Lt. Col. Mustapha Debboun, a medical entomologist at the Army Medical Center and School in Fort Sam Houston, Texas.

DEET actually has a good safety record, asserts Debboun, who heads the armed forces' repellent committee and is co-editor of the forthcoming book *Repellents*, the first overall look at the field. The compound is used hundreds of millions of times worldwide each year, with only about 50 known reports of severe dermatitis or seizures since it came into use - problems usually attributed to gross overuse, if they can be clearly connected to the product at all. "But if soldiers are afraid of it, we need to look for alternatives," says Debboun.

Some researchers are turning to folk remedies--and finding a few that may work,

The military issues DEET, the most widely used repellent, but not all soldiers like it.

Auklets produce a natural repellent called aldehydes. Repellents are not trivial for the birds; the insects are so vicious that they can threaten a breeding colonies' existence. During buggy times, one can smell the citrusy aldehydes a kilometer away from the colony.

Anopheles gambiae is the principle vector of malaria in Africa. Malaria is a parasitic disease that infects 300 to 500 million people in the world every year.

at least to a degree. The U.S. Department of Agriculture (USDA), which has traditionally led American research at the relatively modest funding rate of about $1 million per year, has shown that many plant oils, including clove, peppermint, geranium, and catnip, may repel mosquitoes. Botanists have long known that plants produce compounds to combat pests that might eat them; entomologists speculate that there may be a chemical spillover effect on those that eat us.

For example, last year USDA botanist Charles Bryson showed that his grandfather was right when he shoved American beautyberry leaves under his draft animals' harnesses to repel biting flies. Bryson and colleagues reported in the Journal of Agricultural and Food Chemistry that they have isolated five compounds that repel bugs including *Aedes aegypti*, the mosquito species that carries yellow fever.

Animals may also employ natural repellents. Recently, Paul Weldon, an animal behaviorist at the Smithsonian Institution in Washington, D.C., observed that some monkey species rub themselves with millipedes that secrete benzoquinones, compounds shown in the lab to repel insects.

Other creatures, from giraffes to gaurs, may produce their own repellents. Auklets on arctic islands exude aldehydes that drive off ticks and mosquitoes and kill lice in lab experiments, according to a paper last year in the *Journal of Medical Entomology* by ecologist Hector Douglas of the University of Alaska, Fairbanks.

But there are many obstacles between identifying natural repellents and deriving marketable products from them. A widely cited 2003 study in *The New England Journal of Medicine* by Chapel Hill, North Carolina, dermatologist Mark Fradin shows that many "botanicals," including popular citronella formulations such as Avon Skin-So-Soft, work--but only for 3 to 20 minutes. Part of the problem is that the compounds are usually quite volatile and evaporate unless constantly replaced. Some natural oils will repel bugs for up to 2.5 hours, but only if they are distilled down to something near the pure stuff, which is usually stinky and toxic, says Don Barnard, a USDA entomologist. Aldehydes, for example, smell nice in low doses but are hard to bear once purified. High doses also may corrode people's mucous membranes and livers.

Researchers continue to hunt for natural repellents, including those produced by humans. Ulrich Bernier, a chemist at USDA, has identified about 275 substances in human sweat, including aldehydes similar to those produced by auklets, along with ketones, fatty acids, and ammonia. Everyone sweats out the same chemicals, but the concentrations and proportions may vary widely among individuals--possibly the key to why bugs eat some folks alive but leave others alone.

One group at the United Kingdom's government-funded Rothamsted Research has combined human and animal research. Biochemist John Pickett has shown that some cattle exude powerful compounds that keep biting flies off themselves and nearby animals. The tendency to produce the substances appears to be inherited through the mother, he says. Rothamsted chemical ecologist James Logan says humans produce similar compounds.

The discovery process is slowed, however, not only by the complexity of how aromas interact with one another, but also by the varying tastes of different insect species, strains within species, and even individual insects. Says Bernier: "We're

Malaria Facts

▪ 41% of the world's population lives in areas where malaria can be transmitted.

▪ An estimated 700,000 to 2.7 million people die from malaria each year, 75% of them are African children.

▪ The average cost for potentially life-saving treatments of malaria are estimated to be $0.13 to $2.68.

People with little or no immunity to malaria, such as young children, pregnant women, and people who travel from areas with no malaria to areas where malaria is endemic are more likely to become severely ill and die.

The International Federation of Red Cross and Red Crescent Societies began distributing over 2 million long-lasting insecticide-treated mosquito nets in Niger in 2005 in an effort to protect 3.5 million children from malaria.

just beginning to understand: Insects are like picky wine drinkers. They like something or not, based on very subtle combinations of qualities."

Testing troubles: Repellents' exact modes of operation remain mysterious. A few months ago, Jerome Klun, a USDA entomologist, finally showed in the *Journal of Medical Entomology* that vapors from DEET and some other substances function mainly by traveling to insects' olfactory receptors, as opposed to affecting the insects when they touch skin. However, Klun says it is still unclear whether the substances create an unpleasant sensation for insects, mask attractive odors, or work in some other way. To discover repellents without knowing why they work, one new Army initiative uses computers to identify molecules similar to existing repellents, then synthesizes and tests the compounds. From this, a team has come up with at least four compounds now under investigation.

But even if compounds prove interesting, documenting their effectiveness is often complicated. For example, a few new repellents are now on the market, but it's hard to compare them to each other, or to DEET. One substance is para-menthane-3,8-diol (PMD), commonly known as oil of lemon eucalyptus. Derived from the Australian lemon- scented gum tree and marketed in China for years, it appeared last year in the United States under the brand name Repel. In some tests, 20% PMD appears to be nearly as effective as most of the 240-some standard DEET products--perhaps better. Other studies, however, suggest that PMD is weaker than DEET. One problem is that there are 3000 species of mosquitoes alone, and most repellents work better on some than on others. But many tests using caged mosquitoes are conducted using only one or two species. And in the field, insects' tastes may vary dramatically by concentration of the repellent, time of day, temperature, humidity, individual volunteers, and insect species themselves--variables that few researchers try to control for.

Two other promising repellents are newly available in the US: Picaridin, a synthetic derivative of pepper marketed under the name Cutter Advanced, and IR3535, a derivative of a single amino acid, beta-alanine, now sold in a beefed-up version of Skin-So-Soft. However, research on them suffers similar complications. "What's best? It sounds like a simple question, but there really is no easy answer," says Robert Novak, a medical entomologist at the Illinois Natural History Survey.

Perhaps the most sophisticated repellent effort, aimed at stages from basic biology to field tests to marketing, is a 5-year project begun last September and funded by the Bill and Melinda Gates Foundation. The $8.5 million budget is comparable to that of USDA and the U.S. military combined. Following their 2001 identification of the genes for the 80-some olfactory receptors used by malaria-carrying *Anopheles gambiae* mosquitoes, two labs in the United States have begun running tests with hundreds of substances to observe which cause receptors either to fire or become blocked.

Yale's Carlson has been working in part with compounds taken from human sweat and tested in fruit flies that express mosquito receptors. He has already sent a half-dozen candidate compounds on to the next stage: the lab of behavioral entomologist Willem Takken at the University of Wageningen in the Netherlands. After again measuring whether receptors fire, this time in the mosquitoes' antennae, he employs wind-tunnel-like olfactometers, in which insects can choose to follow or avoid certain paths from which different smells emanate.

DOH WNV Contacts

Toll Free Info Line
1-866-78VIRUS

Publication Requests
Cyndi Free
360-236-3384
cyndi.free@doh.wa.gov

Mosquito and Bird Surveillance
Jo Marie Brauner
360-236-3064
jomarie.brauner@doh.wa.gov

Horse Surveillance
Ron Wohrle
360-236-3369
ron.wohrle@doh.wa.gov

Aquatic Mosquito Control NPDES Permit
Ben Hamilton
360-236-3364
benjamin.hamilton@doh.wa.gov

WNV in Humans
Local Health Jurisdiction
or
DOH Communicable Disease Epidemiology
206-418-5500 or
877-539-4344

News Releases/ Media Response Assistance
Donn Moyer
360-236-4076
donn.moyer@doh.wa.gov
or
Tim Church
360-236-4077
tim.church@doh.wa.gov

WNV Program Management
Maryanne Guichard
360-236-3391
maryanne.guichard@doh.wa.gov

WNV Coordinator
Dorothy Tibbetts
360-236-3361
dorothy.tibbetts@doh.wa.gov

Compounds that show promise will be sent to Tanzania, where a greenhouselike biosphere about half the size of a football field is now under construction. Here, human volunteers will test candidate repellents against free-flying mosquitoes in a semicontrolled environment. Top picks will go to Gambia, where researchers will do full field tests in villages--then, hopefully, to market by 2011.

Takken, Carlson, and Laurence J. Zwiebel of Vanderbilt University, emphasize that they are looking not just for repellents but also attractants. They hope to develop a "push-pull" system that will employ repellents to drive mosquitoes away from people's beds or other feeding spots and attractants to draw them into insecticide-laced traps in distant parts of houses or villages. Zwiebel says the key will be to keep the system cheap and to use sales of repellents in richer countries to subsidize use in poorer ones. "The Third World can't afford what we spend to protect our backyard barbecue," says Zwiebel. "But they really need repellents."

View this *Science* article in it's entirety at the Armed Forces Pest Management Board Web site, http://www.afpmb.org/bulletin/vol26/Krajick%202006.pdf.

Washington environmental surveillance summary

Reported to DOH as of July 27, 2006

	Horses*		Birds**		Sentinel Flocks***		Mosquito Pools****	
County	Tested	Positive	Tested	Positive	Tested	Positive	Tested	Positive
Adams	0	0	1	0	0	0	0	0
Asotin	0	0	0	0	0	0	0	0
Benton	2	0	3	0	136	0	117	0
Chelan	0	0	2	0	0	0	0	0
Clallam	0	0	0	0	0	0	0	0
Clark	1	0	0	0	0	0	5	0
Columbia	0	0	1	0	0	0	0	0
Cowlitz	0	0	6	0	0	0	39	0
Douglas	0	0	0	0	0	0	0	0
Ferry	0	0	0	0	0	0	0	0
Franklin	0	0	1	0	0	0	0	0
Garfield	0	0	0	0	0	0	0	0
Grant	0	0	1	0	0	0	0	0
Grays Harbor	0	0	3	0	0	0	0	0
Island	0	0	8	0	0	0	0	0
Jefferson	0	0	4	0	0	0	0	0
King	0	0	4	0	0	0	1	0
Kitsap	0	0	0	0	0	0	0	0
Kittitas	0	0	1	0	0	0	0	0
Klickitat	0	0	1	0	0	0	0	0
Lewis	0	0	1	0	0	0	0	0
Lincoln	0	0	0	0	0	0	0	0
Mason	0	0	5	0	0	0	0	0
Okanogan	0	0	0	0	0	0	0	0
Pacific	0	0	0	0	0	0	0	0
Pend Oreille	0	0	0	0	0	0	0	0
Pierce	0	0	25	0	0	0	0	0
San Juan	1	0	0	0	0	0	0	0
Skagit	0	0	2	0	0	0	0	0
Skamania	0	0	0	0	0	0	0	0
Snohomish	1	0	11	0	0	0	15	0
Spokane	1	0	4	0	0	0	0	0
Stevens	0	0	2	0	0	0	0	0
Thurston	0	0	9	0	0	0	0	0
Wahkiakum	0	0	0	0	0	0	0	0
Walla Walla	1	0	4	0	0	0	0	0
Whatcom	1	0	0	0	0	0	0	0
Whitman	0	0	4	0	0	0	0	0
Yakima	0	0	3	0	28	0	196	0
Totals	8	0	106	0	164	0	373	0

*A total of 11 horses have been tested for West Nile virus. An additional 3 horse tested negative, but were not included in the table because county/state information was not available. WADDL Report: July 18, 2006.
**A total of 107 birds have been tested for West Nile virus; 1 specimen was from out-of-state. WADDL Report: July 20, 2006.
*** Sentinel Chicken Sera tested by Benton MCD Report: July 25, 2006.
**** Pools tested by USACHPPM-West Report: July 14, 2006, Cowlitz MCD Report: July 13, 2006 and Benton MCD Report: July 25, 2006.

View the WNV Avian Mortality Report at http://www.doh.wa.gov/ehp/ts/Zoo/WNV/Newsletters/dbreport/dbreport.pdf.